Last time: bacterial growth in chemostat

nutrient influx: $j_0 = n_0 \cdot \mu$ ← dilution rate

↑ nutrient concent at inflow

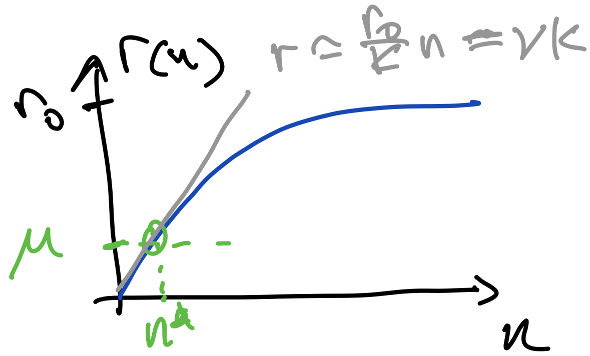
$$\begin{cases} \dot\rho = r(n)\rho - \mu\rho \\ \dot n = n_0\mu - n\cdot\mu - r(n)\rho/Y \end{cases}$$ ← biomass yield $= \frac{\delta\rho}{\delta n}$

mass conservation: $\dot\rho + Y\dot n = \mu[(n_0 - n(t))Y - \rho(t)]$

for non-trivial steady state sol'n ($\rho^* > 0$, $n^* > 0$)

$\dot\rho = 0$ & $\dot n = 0$ → $\rho^* = (n_0 - n^*)\cdot Y$ (indep't of $r(n)$)

value of $n^*$ from $\mu = r(n^*)$




Monod growth law:

$$r(n) = r_0 \frac{n}{n+K}$$

$$\rightarrow \frac{n^*}{K} = \frac{\mu}{r_0 - \mu} \xrightarrow[\text{(typical)}]{\mu \ll r_0} \frac{\mu}{r_0}$$

$$\frac{n^*}{n_0} = \frac{\mu K}{r_0 n_0} = \frac{\mu}{\nu n_0} \equiv \eta \quad \text{(dimensionless parameter)}$$

$$\rho^* = \underbrace{n_0 Y}_{\rho_0} \left(1 - \frac{n^*}{n_0}\right) = \rho_0 \cdot (1-\eta)$$

$\rho_0$: max density attainable.

$\eta \to 1$: $\rho^* \to 0$ (washout)

$\eta \to 0$: $n^* \to 0$, $\rho^* \to \rho_0$ (Complete conversion)

⇒ can estimate $K$ by seeing how $\rho^*$ depends on $n_0$

but may be diff in practice due to proximity to washout

- Chemostat most stable when $\eta \ll 1$

in this limit, $\frac{n^*}{n_0} \simeq \eta \ll 1$.

$$\rho^* = (n_0 - n^*) Y \simeq n_0 Y \equiv \rho_0$$

$\rightarrow$ nutrient inflow mostly goes to biomass

(difficult to measure $n^*$, or $\rho_0 - \rho^*$)

- opposite limit $\eta \to 1$ (approaching wash out)

$$\frac{n^*}{n_0} \simeq \eta \to 1, \quad \text{(e.g. reduce } n_0\text{)}$$

$$\rho^* = (n_0 - n^*) Y = (1-\eta) \rho_0 \longrightarrow 0$$

(Can estimate K, may be difficult to maintain)

b) Dynamics (relation to logistic growth model)

$$\dot{\rho} = (r(n) - \mu)\rho = (\nu n - \mu)\rho$$

$$\dot{n} = \mu(n_0 - n) - r(n)\rho/Y = \mu(n_0 - n) - \nu n \rho / Y.$$

[Compare to the damped predator-prey system (Sec A3)

$$\dot{p} = r p (1 - p/\tilde{p}) - b p q$$

$$\dot{q} = c p q - \mu q$$

nutrient $(n) \leftrightarrow$ prey $(p)$

cell $(\rho) \leftrightarrow$ predator $(q)$

$c \leftrightarrow \nu$; $b \leftrightarrow \nu/Y$.

main difference:

- prey replicates at rate $r \cdot (1-\rho/\tilde{\rho})$
- nutrient injected at rate $\mu(n_0 - n)$

HW: In the limit $\eta \lesssim 1$ (near washout) dynamics converges to rapidly to

$$\rho(t) = [n_0 - n(t)] \cdot Y \quad \text{(mass conservation)}$$

Slow mode: $$\frac{d\rho}{dt} = (\nu n(t) - \mu)\,\rho = [\nu(n_0 - \rho(t)/Y) - \mu]\,\rho$$
$$= [(\nu n_0 - \mu) - \nu \rho(t)/Y]\,\rho$$

$$\boxed{\frac{d\rho}{dt} = (r - \rho/\tilde{\rho}) \cdot \rho}$$

→ recovers logistic eqn with effective "growth rate"

$$r = \nu n_0 - \mu = \mu \cdot (\eta^{-1} - 1) \ll 1 \quad \text{for } \eta \lesssim 1$$

and "carrying capacity"

$$\tilde{\rho} = \frac{(\nu n_0 - \mu) Y}{\nu} = \rho_0 (1 - \eta) \ll \rho_0$$

(logistic eqn recovered here because it is leading order expansion in $\rho$ when $\tilde{\rho}$ is small)

# II B. CR Model of Competition & Coexistence

## 1. Two-Species interaction

a) 2-Species growing on a single substrate

chemostat with dilution rate $\mu$

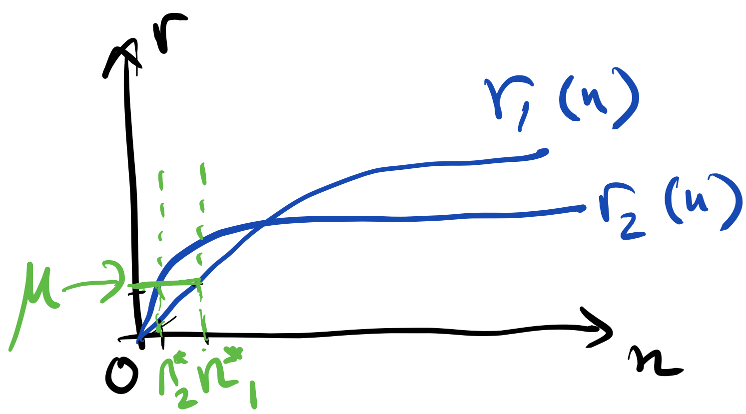
$$\dot{\rho}_1 = r_1(n)\rho_1 - \mu\rho_1$$
$$\dot{\rho}_2 = r_2(n)\rho_2 - \mu\rho_2$$
$$\dot{n} = \mu(n_0 - n) - r_1(n)\rho_1/Y - r_2(n)\rho_2/Y$$

$$r_i(n) = r_i^0 \frac{n}{n+K_i}$$

Steady state:

$\mu = r_1(n^*)$, $\mu = r_2(n^*)$

→ Cannot be satisfied simultaneously unless
$r_1(n) = r_2(n)$




Sol'n: $\mu = r_i(n^*)$, with $\rho_i \neq 0$, while $\rho_{j\neq i} = 0$.

→ i.e. only one species survives in steady state

HW: Surviving species is one with lower $n_i$

[approach: Assume one of the species goes extinct, e.g. $\rho_2 = 0$.
check for stability for small $\rho_2 > 0$.]

b) two species (of densities $\rho_1$ $\rho_2$) growing on two nutrients (of concentrations $n_A, n_B$)

- chemostat with dilution rate $\mu$.
- nutrient influx ($j_A^0 = \mu n_A^0$, $j_B^0 = \mu n_B^0$)

Uptake of multiple nutrients:

- substitutable (e.g. glucose vs. glycerol)
- essential (e.g. glucose + ammonium)

Substitutable nutrients:

- Many substrates co-utilized; GR approx additive

i.e. $r_i(n_A, n_B) \simeq r_i^0 \frac{n_A}{K_{i,A}} + r_i^0 \frac{n_B}{K_{i,B}}$

$\equiv \nu_{iA} n_A + \nu_{iB} n_B$

[Hermsen et al MSB 2014]

- Some combo of substrates hierarchically utilized

i.e., $r_i(n_A, n_B) = \max\{r_i(n_A), r_i(n_B)\}$

essential nutrients: $r_i \simeq \left(\frac{1}{\nu_{iA} n_A} + \frac{1}{\nu_{iB} n_B}\right)^{-1}$

→ will focus on substitutable, co-utilized nutrients in lectures; others in HW.

Dynamical equations:

$$\dot\rho_1 = (\nu_{1A} n_A + \nu_{1B} n_B)\rho_1 - \mu\rho_1$$

$$\dot\rho_2 = (\nu_{2A} n_A + \nu_{2B} n_B)\rho_2 - \mu\rho_2$$

$$\dot n_A = \mu(n_A^0 - n_A) - \nu_{1A} n_A \rho_1 / Y_A - \nu_{2A} n_A \rho_2 / Y_A$$

$$\dot n_B = \mu(n_B^0 - n_B) - \nu_{1B} n_B \rho_1 / Y_B - \nu_{2B} n_B \rho_2 / Y_B$$

assumption made: yield is species independent,

$Y_\alpha$ can be scaled out

$\nu_{i\alpha}/Y_\alpha = \tilde\nu_{i\alpha}$

$n_\alpha Y_\alpha = \tilde n_\alpha$

but different substrate can contribute quite differently to biomass, e.g. glucose has 6C, glycerol only 3C

* Steady state soln (for $\rho_1^* \neq 0$, $\rho_2^* \neq 0$)

$\dot\rho_1 = 0$. $\quad \nu_{1A} n_A + \nu_{1B} n_B = \mu$

$\dot\rho_2 = 0$ $\quad \nu_{2A} n_A + \nu_{2B} n_B = \mu$

$$\begin{bmatrix} \nu_{1A} & \nu_{1B} \\ \nu_{2A} & \nu_{2B} \end{bmatrix} \begin{bmatrix} n_A \\ n_B \end{bmatrix} = \begin{bmatrix} \mu \\ \mu \end{bmatrix}$$

Recall linear algebra

$$M \cdot \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} b_1 \\ b_2 \end{bmatrix} \rightarrow \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = M^{-1} \cdot \begin{bmatrix} b_1 \\ b_2 \end{bmatrix}$$

$$M = \begin{bmatrix} m_{11} & m_{12} \\ m_{21} & m_{22} \end{bmatrix}$$

$$M^{-1} = \frac{1}{\det M} \begin{bmatrix} m_{22} & -m_{12} \\ -m_{21} & m_{11} \end{bmatrix}$$

$$\begin{bmatrix} n_A^* \\ n_B^* \end{bmatrix} = \frac{1}{\det(\nu)} \begin{bmatrix} \nu_{2B} & -\nu_{1B} \\ -\nu_{1A} & \nu_{1A} \end{bmatrix} \begin{bmatrix} \mu \\ \mu \end{bmatrix} = \frac{\mu}{\det(\nu)} \begin{bmatrix} \nu_{2B} - \nu_{1B} \\ \nu_{1A} - \nu_{2A} \end{bmatrix} \sim O(\mu/\nu)$$

Note: nutrient levels set by $\nu_{ij}$ and $\mu$. not dependent on $\rho_i$, nor $n_i^0$ (cf. chemostat)

$\rho_1^*, \rho_2^*$ found from $\dot{n}_A = 0, \dot{n}_B = 0$

$$\nu_{1A} n_A^* \rho_1^* + \nu_{2A} n_A^* \rho_2^* = \mu (n_A^0 - n_A^*) Y_A$$

$$\nu_{1B} n_B^* \rho_1^* + \nu_{2B} n_B^* \rho_2^* = \mu (n_B^0 - n_B^*) Y_B$$

$$\underbrace{\begin{bmatrix} \nu_{1A} & \nu_{2A} \\ \nu_{1B} & \nu_{2B} \end{bmatrix}}_{\nu^T} \begin{bmatrix} \rho_1^* \\ \rho_2^* \end{bmatrix} = \mu \begin{bmatrix} \left(\frac{n_A^0 - n_A^*}{n_A^*}\right) Y_A \\ \left(\frac{n_B^0 - n_B^*}{n_B^*}\right) Y_B \end{bmatrix},$$

$$\begin{bmatrix} \rho_1^* \\ \rho_2^* \end{bmatrix} = \frac{\mu}{\det(\nu^T)} \begin{bmatrix} \nu_{2B} & -\nu_{2A} \\ -\nu_{1B} & \nu_{1A} \end{bmatrix} \cdot \begin{bmatrix} \phantom{x} \end{bmatrix} = \frac{\mu}{\det(\nu^T)} \begin{bmatrix} \nu_{2B} \frac{n_A^0 - n_A^*}{n_A^*} Y_A - \nu_{2A} \frac{n_B^0 - n_B^*}{n_B^*} Y_B \\ -\nu_{1B} \frac{n_A^0 - n_A^*}{n_A^*} Y_A + \nu_{1A} \frac{n_B^0 - n_B^*}{n_B^*} Y_B \end{bmatrix}$$

from above: $n_A^* = \mu (\nu_{2B} - \nu_{1B}) / \det(\nu)$ $\rightarrow$ $1/n_A^* = \det(\nu) / [\mu (\nu_{2B} - \nu_{1B})]$

$n_B^* = \mu (\nu_{1A} - \nu_{2A}) / \det(\nu)$ $\quad$ $1/n_B^* = \det(\nu) / [\mu (\nu_{1A} - \nu_{2A})]$

$$\begin{bmatrix} \rho_1^* \\ \rho_2^* \end{bmatrix} = \begin{bmatrix} \frac{(n_A^0 - n_A^*) Y_A}{1 - \nu_{1B}/\nu_{2B}} + \frac{(n_B^0 - n_B^*) Y_B}{1 - \nu_{1A}/\nu_{2A}} \\ \frac{(n_A^0 - n_A^*) Y_A}{1 - \nu_{2B}/\nu_{1B}} + \frac{(n_B^0 - n_B^*) Y_B}{1 - \nu_{2A}/\nu_{1A}} \end{bmatrix};$$

$\det \nu = \det \nu^T$

Note 1: $\rho_1^* + \rho_2^* = (n_A^0 - n_A^*) Y_A + (n_B^0 - n_B^*) Y_B$ — mass conservation

Note 2: if $\mu \to 0$, then $n_A^*, n_B^* \to 0$ (little nutrient left

$\rho_1^*, \rho_2^*$ depend on $(n_A^0 Y_A, n_B^0 Y_B)$ + $\nu_{i\alpha}$

Note 3: if $n_A^0 - n_A^* \to 0$, $n_B^0 - n_B^* \to 0$ (i.e. $n_A^0 \to \frac{\mu (\nu_{2B} - \nu_{1B})}{\nu_{1A}\nu_{2B} - \nu_{1B}\nu_{2A}}$ )

then $\rho_1^* \to 0$, $\rho_2^* \to 0$ (washout limit of chemostat)

Goal: Understand dependence of coexistence ($\rho_1 > 0, \rho_2 > 0$) vs. dominance ($\rho_1 > 0, \rho_2 = 0$ or vice versa) or extinction ($\rho_{1,2} = 0$) for diff environmental parameters ($j_A^0 = \mu n_A^0$, $j_B^0 = \mu n_B^0$) and genetic parameters ($\nu_{i\alpha}$, $\mu$)

- find fixed points (if $\rho_i \le 0$, then no coexistence)
- if $\rho_A > 0$, $\rho_B > 0$ exist, determine stability
  - unstable in one direction: phase transition (multi-modality)
  - stable: coexistence occurs
    - → basin of attraction?

A simple limit (weak interaction case):

specialist vs specialist

$n_A \to \rho_1$, $n_B \to \rho_2$

$\nu_{1A} \gg \nu_{2A}$

$\nu_{2B} \gg \nu_{1B}$

→ coexistence. (if not washed out)

Q: as interaction is turned on, to what extent is coexistence stable?

specialist ① vs generalist ②

$n_A \to \rho_1$, $n_B \to \rho_2$

$\nu_{2B} \gg \nu_{1A}, \nu_{1B}$

$\nu_{1B} \ll \nu_{1A}, \nu_{1B}$

??

generalist vs generalist

$n_A \to \rho_1$, $n_B \to \rho_2$

all $\nu_{i\alpha}$ comparable ??

→ General analysis of stability (around $\rho_1^*, \rho_2^*, n_A^0, n_B^*$)

4×4 matrix – not intuitive

→ Short-cut:

effective dynamics of $n_A, n_B$ (Tilman)